

Rejection Under 35 U.S.C. §103

A. Ford and Klein

The Office Action rejects claims 2-11, 14-18 and 20 under 35 U.S.C. §103(a) over U.S. Patent Application Publication No. 2002/0065242 to Ford et al. ("Ford") in view of Klein et al., "Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines," Applied Physics, 78:2396-2398 (2001) ("Klein").

Applicants respectfully traverse the rejection.

Claim 2 recites "[a] method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, said method comprising the steps: (i) providing a hydrophobic surface, (ii) immobilizing hydrophilic macromolecules on the hydrophobic surface, (iii) exposing the hydrophilic macromolecules immobilized on the hydrophobic surface to hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules" (emphasis added). Ford and Klein do not disclose or suggest such a method.

It is undisputed that neither Ford nor Klein discloses or suggests the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Accordingly, the propriety of the rejection turns on whether one of ordinary skill in the art would have been motivated to combine the teachings of Ford and Klein as proposed in the Office Action. A *prima facie* case of obviousness based on a proposed combination of references (e.g., replacing the hydrophilic substrate of Ford with the hydrophobic substrate of Klein) will only stand if one of ordinary skill would have had a reasonable expectation of success upon making the modification. See, e.g., MPEP §2143.02 (citing *In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986)).

In the previous response, Applicants asserted that one of ordinary skill in the art would not expect that the method of Ford would function employing a hydrophobic substrate

as disclosed in Klein because of the known tendency of hydrophilic species to adsorb non-specifically and irreversibly to hydrophobic substrates. That is, one of ordinary skill in the art would not expect to be able to control the deposit of hydrophilic species on a hydrophobic substrate and, thus, one of ordinary skill in the art would not expect success upon combining Ford and Klein as proposed in the Office Action.

In support of Applicants arguments, reference was made to U.S. Patent No. 5,516,703 to Caldwell et al. ("Caldwell"), which demonstrates that hydrophilic species adsorb non-specifically to hydrophobic substrates. *See, e.g.*, column 1, lines 44 to 59. The Office Action asserts that Caldwell does not provide such a demonstration. *See* Office Action, page 9. Rather, the Office Action asserts that Caldwell's teachings are limited to the non-specific adsorption of antibodies to hydrophobic substrates and, thus, would not discourage a skilled artisan from attempting to employ the hydrophilic species of Ford (gold nanoparticles) with a hydrophobic substrate. *See* Office Action, page 9. While Applicants do not necessarily agree with the Office Action's characterization of Caldwell, Applicants have attached hereto a further reference demonstrating that one of ordinary skill in the art would expect hydrophilic gold nanoparticles to adsorb non-specifically to a hydrophobic substrate. *See* Fan, H., et al., "Adsorption of Surface-Modified Colloidal Gold Particles onto Self-Assembled Monolayers: A Model System for the Study of Interactions of Colloidal Particles and Organic Surfaces," *Langmuir* 1997, 13, 119-121 ("Fan").

As discussed during the November 27, 2007 Personal Interview, Fan describes the adsorption of gold nanoparticles to self-assembled monolayers. In particular, Fan describes the manner in which hydrophilic gold nanoparticles adsorb to surfaces having differing degrees of hydrophobicity. As can be seen, for example, from FIG. 3 of Fan, the more hydrophobic a surface is, the greater the adsorption of gold particles. As stated in Fan, "results confirm that the colloids studied adsorb from the aqueous solution more extensively

to hydrophobic surfaces." *See* Fan, Abstract. Moreover, "adsorption of colloidal gold particles onto SAMs indicate that adsorption of colloidal particles onto organic surfaces from aqueous suspensions follows thermodynamic predictions to a considerable extent: more colloidal particles adsorb to more hydrophobic organic surfaces." *See* Fan, page 121 (emphasis added). Thus, as previously asserted, one of ordinary skill in the art would not expect to be able to control the deposit of hydrophilic species on a hydrophobic substrate and, thus, one of ordinary skill in the art would not expect success upon combining Ford and Klein as proposed in the Office Action

Applicants surprisingly discovered that exposure of a hydrophilic species (e.g., an aqueous solution of gold nanoparticles) to a hydrophobic substrate (e.g., polystyrene) on which hydrophilic macromolecules are immobilized provides a desirable result. Namely, the hydrophilic species binds specifically (i.e., almost exclusively) to the hydrophilic molecule, and not the hydrophobic substrate. *See, e.g.*, present specification, pages 10 to 11. That is, the hydrophilic species does not bind non-specifically to the hydrophobic substrate as would have been expected in view of past experience relating to the binding of hydrophilic species to hydrophobic substrates.

As neither Ford nor Klein discloses or suggests the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species, and one of ordinary skill in the art would not expected success upon combining Ford and Klein as proposed in the Office Action, the combination of Ford and Klein would not have rendered obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford and Klein. Claims 3-11, 14-18 and 20 depend from claim 2 and, thus, also would not have been rendered obvious by Ford and Klein. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

B. Ford, Klein and Tajima

The Office Action rejects claims 12 and 13 under 35 U.S.C. §103(a) over Ford in view of Klein and U.S. Patent No. 4,649,071 to Tajima et al. ("Tajima"). Applicants respectfully traverse the rejection.

Claim 2 is set forth above. For the reasons discussed above, Ford and Klein do not disclose or suggest the method of claim 2. Tajima does not remedy the deficiencies of Ford and Klein. Tajima is cited for its alleged disclosure of the water contact angle of polystyrene. *See* Office Action, page 4. However, Tajima, like Ford and Klein fails to disclose or suggest the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Accordingly, the combination of Ford, Klein and Tajima fails to render obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford, Klein and Tajima. Claims 12 and 13 depend from claim 2 and, thus, also would not have been rendered obvious by Ford, Klein and Tajima. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

C. Ford, Klein and Berning

The Office Action rejects claim 19 under 35 U.S.C. §103(a) over Ford in view of Klein and Berning et al., "<sup>198</sup>Au Labeled Hydroxymethyl Phosphines as Models for Potential Therapeutic Pharmaceuticals," *Nuclear Medicine and Biology*, 25: 577-583 (1998) ("Berning"). Applicants respectfully traverse the rejection.

Claim 2 is set forth above. For the reasons discussed above, Ford and Klein do not disclose or suggest the method of claim 2. Berning does not remedy the deficiencies of Ford and Klein. Berning is cited for its alleged disclosure of tris(hydroxymethyl)phosphine-gold

nanoparticles. *See* Office Action, page 4. However, Berning, like Ford and Klein fails to disclose or suggest the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species.

Accordingly, the combination of Ford, Klein and Berning fails to render obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford, Klein and Berning. Claim 19 depends from claim 2 and, thus, also would not have been rendered obvious by Ford, Klein and Berning. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

D. Ford and Schueller

The Office Action rejects claims 2, 3 and 14-18 under 35 U.S.C. §103(a) over Ford in view of U.S. Patent Application Publication No. US 2002/0050220 to Schueller et al. ("Schueller"). Applicants respectfully traverse the rejection.

Claim 2 is set forth above. Ford and Schueller fail to disclose or suggest such a method.

The Office Action relies on Ford for its alleged disclosure of providing a hydrophilic substrate, immobilizing hydrophilic nucleic acids on the substrate, and metallizing the immobilized nucleic acids with a hydrophilic species. *See* Office Action, page 5. The Office Action relies on Schueller for its alleged disclosure of immobilizing a hydrophilic nucleic acid on a hydrophobic substrate. *See* Office Action, page 5. It is undisputed that neither Ford nor Schueller discloses or suggests the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species.

Applicants submit that one of ordinary skill in the art would not have expected that the method of Ford would function employing a hydrophobic substrate as disclosed in Schueller, for the reasons discussed above with respect to Ford and Klein.

As neither Ford nor Schueller discloses or suggests the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species, and one of ordinary skill in the art would not have expected success upon combining Ford and Schueller as proposed in the Office Action, the combination of Ford and Schueller would not have rendered obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford and Schueller. Claims 3 and 14-18 depend from claim 2 and, thus, also would not have been rendered obvious by Ford and Schueller. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

E. Ford, Schueller and Tajima

The Office Action rejects claims 12 and 13 under 35 U.S.C. §103(a) over Ford in view of Schueller and Tajima. Applicants respectfully traverse the rejection.

Claim 2 is set forth above. For the reasons discussed above, Ford and Schueller do not disclose or suggest the method of claim 2. Tajima does not remedy the deficiencies of Ford and Schueller. Tajima is cited for its alleged disclosure of the water contact angle of polystyrene. *See* Office Action, page 6. However, Tajima, like Ford and Schueller fails to disclose or suggest the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Accordingly, the combination of Ford, Schueller and Tajima fails to render obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford, Schueller and Tajima. Claims 12 and 13 depend from claim 2 and, thus, also would not have been rendered obvious by Ford, Schueller and Tajima. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

F. Ford, Schueller and Berning

The Office Action rejects claim 19 under 35 U.S.C. §103(a) over Ford in view of Schueller and Berning. Applicants respectfully traverse the rejection.

Claim 2 is set forth above. For the reasons discussed above, Ford and Schueller do not disclose or suggest the method of claim 2. Berning does not remedy the deficiencies of Ford and Schueller. Berning is cited for its alleged disclosure of tris(hydroxymethyl) phosphine-gold nanoparticles. *See* Office Action, page 7. However, Berning, like Ford and Schueller fails to disclose or suggest the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Accordingly, the combination of Ford, Schueller and Berning fails to render obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford, Schueller and Berning. Claim 19 depends from claim 2 and, thus, also would not have been rendered obvious by Ford, Schueller and Berning. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Double Patenting

The Office Action rejects claims 2-6, 11, 15 and 17-19 under the judicially created doctrine of obviousness-type double patenting over claims 1-4, 14-16 and 20 of U.S. Patent Application No. 09/990,049 in view of U.S. Patent No. 5,516,703 to Caldwell et al. Applicants respectfully request that this provisional rejection be held in abeyance until the 049 application issues as a patent or the present application is otherwise indicated to be in condition for allowance.